

Amendment to the Specification

Please amend the paragraph beginning on line 1 of page 66 to incorporate the change noted in the following marked-up paragraph:

The lead structural templates were obtained from the available X-ray structures of the complexes formed between VEGF and anti-VEGF antibodies. The complex structure of VEGF and parental anti-VEGF antibody is designated as 1BJ1, and that formed between VEGF and matured anti-VEGF antibody 1CZ8. The results from 1CZ8 structural template were similar to those from 1BJ1 in the relative ranking order of the scanned sequences. The modeled structure or structure ensemble or ensemble average can be also used for screening sequences. The lead sequence for VH FR123 (SEQ283) is taken from the murine anti-VEGF antibody according to Kabat classification. The HMM built using the single lead sequence was calibrated and used to search human heavy chain germline sequence database and/or human sequence database (including human germlines and humanized sequences) derived from Kabat database (Johnson, G and Wu, TT (2001) Nucleic Acids Research, 29, 205-206). All sequence hits that are above expectation value or E-value are listed and aligned using HAMMER 2.1.1 package. After removing the redundant sequences from the hit list, the remaining hit sequences for the lead HMM form the hit library. The sequence identities of the hit sequences from the human VH germline ranges from 40 to 68% of the lead sequence, whereas the corresponding sequence identities of the hit sequences from human immunoglobulin sequences derived from Kabat database (the database are parsed to fr123 fragment in order to increase the sensitivity of the search and their relative ranking) (other database would be used if the contain the immunoglobulin sequences of human origins) ranging from ~30 to 75%. The evolutionary distances between the hits can be analysed by using the program TreeView1.6.5 (<http://taxonomy.zoology.gla.ac.uk/rod/rod.html>).